

Listing of Claims

Please cancel claims 11-13 and 23-26 without prejudice to subsequence renewal or future prosecution. Please add new claims 32 and 33, and amend the other pending claims as indicated below. This listing of claims will replace all prior versions and listings of claims in the application.

1. **(Currently amended)** A method for treating a metabotropic glutamate disorder, comprising administering to a subject in need thereof, an effective amount of (a) a first one-antagonist which modulates metabotropic glutamate receptor 2 and/or metabotropic glutamate receptor 3, and (b) a second one-antagonist which modulates metabotropic glutamate receptor 5, thereby treating the disorder; wherein the metabotropic glutamate disorder is selected from the group consisting of depression, nicotine addiction, alcohol addiction, opiate addiction, amphetamine addiction, cocaine addiction, and methamphetamine addiction.

2. **(Currently amended)** A method for treating a metabotropic glutamate disorder, comprising administering to a subject in need thereof, an effective amount of (a) a first one-antagonist which modulates metabotropic glutamate receptor 2, and (b) a second one-antagonist which modulates metabotropic glutamate receptor 5, thereby treating the disorder; wherein the metabotropic glutamate disorder is selected from the group consisting of depression, nicotine addiction, alcohol addiction, opiate addiction, amphetamine addiction, cocaine addiction, and methamphetamine addiction.

3. **(Currently amended)** A method for treating a metabotropic glutamate disorder, comprising administering to a subject in need thereof an effective amount (a) a first one-antagonist which modulates metabotropic glutamate receptor 3 and (b) a second one-antagonist which modulates metabotropic glutamate receptor 5, thereby

treating the disorder; wherein the metabotropic glutamate disorder is selected from the group consisting of depression, nicotine addiction, alcohol addiction, opiate addiction, amphetamine addiction, cocaine addiction, and methamphetamine addiction.

4. (previously presented) The method of claim 1, wherein the disorder is an addictive disorder.

5. (original) The method of claim 4, wherein the addictive disorder is nicotine addiction, alcohol addiction, opiate addiction, amphetamine addiction, methamphetamine addiction, or cocaine addiction.

6. (original) The method of claim 4, wherein the addictive disorder is nicotine addiction.

7. (original) The method of claim 4, wherein the addictive disorder is cocaine addiction.

8. (previously presented) The method of claim 1, wherein the disorder is depression.

9. (Previously presented) The method according to claim 1, wherein the antagonist which modulates metabotropic glutamate receptor 5 is 2-methyl-6-(phenylethynyl)-pyridine, and the antagonist which modulates metabotropic glutamate receptor 2 and/or metabotropic glutamate receptor 3 is 2S-2-amino-2-(1S,2S-2-carboxycyclopropan-1-yl)-3-(xanth-9-yl)propionic acid .

10. **(Withdrawn and currently amended)** A combination comprising (a) at least

a first ~~one~~ active ingredient selected from a metabotropic glutamate receptor 2 antagonist and a metabotropic glutamate receptor 3 antagonist, and (b) at least a second active ingredient being a ~~one~~ metabotropic glutamate receptor 5 antagonist, in which the active ingredients are present in each case in free form or in the form of a pharmaceutically acceptable salt, and optionally at least one pharmaceutically acceptable carrier; for simultaneous, separate or sequential use.

11. **(Canceled)** A combination comprising (a) at least one active ingredient which exhibits antagonistic activity against the metabotropic glutamate receptor 2 and the metabotropic glutamate receptor 3, and (b) at least one metabotropic glutamate receptor 5 antagonist, in which the active ingredients are present in each case in free form or in the form of a pharmaceutically acceptable salt, and optionally at least one pharmaceutically acceptable carrier; for simultaneous, separate or sequential use.

12. **(Canceled)** A combination comprising (a) at least one metabotropic glutamate receptor 2 antagonist, and (b) at least one active ingredient which exhibits antagonistic activity against the metabotropic glutamate receptor 3 and the metabotropic glutamate receptor 5, in which the active ingredients are present in each case in free form or in the form of a pharmaceutically acceptable salt, and optionally at least one pharmaceutically acceptable carrier for simultaneous, separate or sequential use.

13. **(Canceled)** A combination comprising (a) at least one metabotropic glutamate receptor 3 antagonist, and (b) at least one active ingredient which exhibits antagonistic activity against the metabotropic glutamate receptor 2 and the metabotropic glutamate receptor 5, in which the active ingredients are present in each case in free form or in the form of a pharmaceutically acceptable salt, and optionally at

least one pharmaceutically acceptable carrier; for simultaneous, separate or sequential use.

14. (withdrawn) The combination according to claim 10 which is a combined preparation or a pharmaceutical composition.

15. (withdrawn) The combination according to claim 10 for simultaneous, separate or sequential use in the treatment of an addictive disorder or depression.

16. (Previously presented) A method of treating a warm-blooded animal having an addictive disorder or depression comprising administering to the animal a combination according to claim 10 in a quantity which is jointly therapeutically effective against an addictive disorder or depression and in which the compounds can also be present in the form of their pharmaceutically acceptable salts; wherein the addictive disorder is selected from the group consisting of nicotine addiction, alcohol addiction, opiate addiction, amphetamine addiction, cocaine addiction, and methamphetamine addiction.

17. (withdrawn) A pharmaceutical composition comprising a quantity, which is jointly therapeutically effective against an addictive disorder or depression, of a pharmaceutical combination according to claim 10 and at least one pharmaceutically acceptable carrier.

18. (canceled)

19. (withdrawn) A commercial package comprising a combination according to claim 10 together with instructions for simultaneous, separate or sequential use thereof in the treatment of an addictive disorder or depression.

20. **(Currently amended)** A method for treating substance abuse, comprising administering to a subject in need thereof, an effective amount of (a) a first one antagonist which modulates mGluR2 and/or mGluR3, and (b) a second one-antagonist which modulates mGluR5, wherein the effective amount is sufficient to diminish, inhibit or eliminate desire for and/or consumption of the substance in the subject.

21. (original) The method of claim 20, wherein the substance is nicotine, alcohol, opiates, amphetamines, methamphetamines, or cocaine.

22. (Previously presented) The method of claim 21, wherein the antagonist which modulates mGluR2 and/or mGluR3 is 2S-2-amino-2-(1S,2S-2-carboxycyclopropan-1-yl)-3-(xanth-9-yl)propionic acid, and the antagonist which modulates mGluR5 is 2-methyl-6-(phenylethynyl)-pyridine.

23. **(Canceled)** A method of screening for an agent that improves the ability of a known inhibitor to at least partially normalize an intracranial self-stimulation (ICSS) threshold of a non-human mammalian subject, comprising: a) affecting the ICSS threshold of the subject; b) administering to the subject, a sufficient amount of the known inhibitor to at least partially normalize the ICSS threshold when administered alone or in combination with another inhibitor, wherein the known inhibitor is an antagonist of at least one of mGluR2, mGluR3, and mGluR5; c) administering to the non-human mammalian subject, an effective amount of a test agent, wherein the test agent is a known or suspected antagonist of at least one of mGluR2, mGluR3, and mGluR5; and d) determining whether the test agent improves the ability of the known inhibitor to at least partially normalize the ICSS threshold, thereby identifying an agent that improves the ability of the known inhibitor to at least partially normalize ICSS threshold.

24. **(Canceled)** The method of claim 23, wherein the method identifies the test agent as an agent effective for the treatment of depression or an addictive disorder.

25. **(Canceled)** The method of claim 23, wherein the known inhibitor is LY341495 or 2-methyl-6-(phenylethynyl)-pyridine.

26. **(Canceled)** The method of claim 23, wherein the test agent improves the ability of the known inhibitor to inhibit desire for and/or consumption of an addictive substance.

27. **(Currently amended)** A method for treating an addictive disorder, comprising: a) administering to a subject in need thereof, an effective amount of a first ~~an~~ antagonist that modulates mGluR5 during a first time period, wherein the first time period is a time period wherein the subject expects to be in an environment wherein, or exposed to stimuli in the presence of which, the subject habitually uses an addictive substance; and b) administering a second ~~an~~ antagonist that modulates mGluR2 and/or 3 during a second time period, wherein the second time period is a time period wherein the subject is suffering from withdrawal and/or depression; wherein the addictive disorder is selected from the group consisting of nicotine addiction, alcohol addiction, opiate addiction, amphetamine addiction, cocaine addiction, and methamphetamine addiction.

28. **(Previously presented)** The method of claim 27, wherein the antagonist that modulates mGluR5 is 2-methyl-6-(phenylethynyl)-pyridine and the antagonist that modulates mGluR2 and/or 3 is 2S-2-amino-2-(1S,2S-2-carboxycyclopropan-1-yl)-3-(xanth-9-yl)propionic acid.

29. **(Currently amended)** A method for treating depressive symptoms and anxiety symptoms of depression, comprising administering to a subject in need thereof, an effective amount of (a) a first ~~an~~ antagonist which modulates metabotropic glutamate receptor 2 and metabotropic glutamate receptor 3, and (b) a second ~~an~~ antagonist which modulates metabotropic glutamate receptor 5, thereby treating the depressive symptoms and anxiety symptoms of depression.

30. (Previously presented) The method of claim 29, wherein the antagonist of metabotropic glutamate receptor 2 and metabotropic glutamate receptor 3 is administered when the subject experiences depression symptoms, and the antagonist of metabotropic glutamate receptor 5 is administered when the subject experiences anxiety symptoms.

31. (Previously presented) The method of claim 30, wherein the antagonist of metabotropic glutamate receptor 2 and metabotropic glutamate receptor 3 is 2S-2-amino-2-(1S,2S-2-carboxycyclopropan-1-yl)-3-(xanth-9-yl)propionic acid, and the antagonist of metabotropic glutamate receptor 5 is 2-methyl-6-(phenylethynyl)-pyridine.

32. **(New)** The method of claim 1, wherein the first antagonist and the second antagonist are administered to the subject sequentially or simultaneously.

33. **(New)** The method of claim 29, wherein the first antagonist and the second antagonist are administered to the subject sequentially or simultaneously.